

CLAIMS

What is claimed is:

1. A method for estimating a virtual patient's fasting plasma glucose (FPG) level, comprising:
 - determining the virtual patient's basal hepatic production (FPG_0);
 - determining the virtual patient's insulin level (I); and
 - calculating the virtual patient's FPG at time t by solving the differential equation $FPG(t) = FPG_0 / (I * E)$, wherein E is a value representing efficiency of insulin use.
2. The method of claim 1, wherein E is scaled such that $E = 1$ in the absence of diabetes and $0 \leq E \leq 1$ in the presence of diabetes.
3. The method of claim 1, wherein for type 2 diabetes, a differential equation representing E is:

$$E(DF_2) = \left(a + b / (1 + (DF_2 / c)^d) \right)^{\frac{1}{2}},$$
 wherein DF_2 is a type 2 diabetes feature.
4. The method of claim 3,

wherein $DF_2(t) = \left(1 - \exp \left(-a * IGT(\xi_3) / \left(1 + \exp \left(-\frac{(t-b)}{c} \right) \right) \right) \right) * RBMI(BMI) / \xi_2$, wherein a , b , and c are constants, IGT is an impaired glucose tolerance value, and $RBMI$ is the relative risk associated with a person's body mass index (BMI).

5. The method of claim 4, wherein the *RBMI* is represented by:

$$RBMI(BMI) = a + b / \left(1 + e^{-(BMI-c)/d} \right).$$

6. The method of claim 4, wherein *IGT* is represented by:

$$IGT(\xi_3) = 2(1 - \xi_3),$$

wherein ξ_3 is a random value designed to cause the occurrence of diabetes in virtual patients to have the same types of interpersonal variations that occur in real people.

7. The method of claim 1, wherein said determining said virtual patient's basal hepatic production in type 2 diabetes includes solving the differential equation

$FPG_0(t) = G(t) * H(DF_2(t))$, wherein $G(t)$ is the degree of insulin resistance in a person with diabetes (H).

8. The method of claim 7, wherein $H(DF_2(t)) = 1 / \left(\text{MAX} \left[E^2(DF_2(t+a)), b \right] \right)$.

9. The method of claim 7, wherein $G(t) = (a + bt^{1.5} - c * t^3 + \Delta_g) / (d - e \exp(-DF_2(t)\xi_2))$,

wherein Δ_g represents a variance of basal hepatic production across individuals.

10. The method of claim 1, wherein

$$I(DF_1, DF_2) = H(DF_2) * E(DF_2) / (1 + \exp((DF_1 - a)/b)).$$

11. A method for estimating if a virtual patient has developed symptoms of type 1 diabetes, comprising:

representing the virtual patient's genetic propensity to develop type 1 diabetes by a family history value *famhis*;

determining if the virtual patient has developed symptoms of type 1 diabetes at time *t* by solving the differential equation

$DF_1(t) = (1 - \exp(-\exp(a + bt + ct^2 + dt^3 + et^4 + ft^5)) * \text{famhis}) / \xi_1$, wherein *a*, *b*, *c*, *d*, *e*, and *f* are constants and ξ_1 is a random value.

12. A method for estimating if a virtual patient has developed symptoms of type 2 diabetes, comprising:

determining the virtual patient's relative risk associated with body mass index (RBMI);

determining the virtual patient's impaired glucose tolerance level (IGT); and

determining if the virtual patient has developed symptoms of type 2 diabetes at time *t* by

solving the differential equation

$$DF_2(t) = \left(1 - \exp \left(-a * IGT(\xi_3) / \left(1 + \exp \left(-\frac{(t-b)}{c} \right) \right) \right) \right) * RBMI(BMI) / \xi_2, \text{ wherein } a,$$

b, and *c* are constants.

13. The method of claim 12, wherein the RBMI is represented by:

$$RBMI(BMI) = a + b / (1 + e^{-(BMI-c)/d}), \text{ wherein } BMI \text{ is the virtual patient's body mass index.}$$

14. The method of claim 12, wherein IGT is represented by:

$$IGT(\xi_3) = 2(1 - \xi_3),$$

wherein ξ_3 is a random value.

15. A method for estimating a virtual patient's hemoglobin A_{1c} (HbA_{1c}), comprising:

determining said virtual patient's fasting plasma glucose (FPG); and

calculating said virtual patient's hemoglobin A_{1c} by solving the

equation $HbA_{1c}(FPG) = a * FPG - b$, wherein a and b are constants.

16. A method for estimating a virtual patient's randomly measured blood glucose (RPG), comprising:

determining said virtual patient's fasting plasma glucose (FPG); and

calculating said virtual patient's randomly measured blood glucose by solving the

equation $RPG(FPG) = (a + b / (1 + \exp(-(FPG - c)d))) * \exp \Delta_{RPG}$, wherein a , b , c , and d are constants, and Δ_{RPG} is an uncertainty value.

17. A method for estimating a virtual patient's tolerance to an oral glucose load at age t , comprising:

determining the virtual patient's fasting plasma glucose (FPG);

determining the virtual patient's body mass index (BMI);

determining the virtual patient's systolic blood pressure (SBP);

determining the virtual patient's triglyceride level (TRI); and

calculating the virtual patient's tolerance to an oral glucose load at age t by solving the equation:

$$OGT(t) = a * FPG(t) + bt + cBMI(t) + dSBP(t) + eTRI(t) - f + VAR_{OGT}.$$

18. The method of claim 17, wherein said determining the virtual patient's SBP may include multiplying a peripheral resistance for the virtual patient by a diabetes blood pressure factor ($DiabBP$), which is a function of a diabetes feature and higher for people with more severe diabetes.

19. A method for estimating a virtual patient's thirst level at time x , comprising:
determining the virtual patient's fasting plasma glucose (FPG);
determining a standard deviation (SD_{thirst}) of the degree of thirst experienced by an individual; and

calculating the virtual patient's thirst level at time x and age t by solving the equation

$$Thirst(x, FPG(t)) = \frac{1}{\sqrt{2\pi SD_{thirst}}} \exp\left(-\left(\frac{x - MeanSym_{thirst}(FPG(t))}{2SD_{thirst}}\right)^2\right).$$

20. A method for estimating the probability of occurrence of diabetic ketoacidosis events (DKA_{time}) for a virtual patient, comprising:

determining the virtual patient's insulin level if left untreated; and

calculating the virtual patient's probability of occurrence of diabetic ketoacidosis events by solving the equation $DKA_{time} = \text{Max}(a/(1 + \exp(I_{untreated} - b)/c)d)$, wherein a , b , c , and d are constants.

21. A method for estimating the probability of a moderate or severe hypoglycemic event (*HypoGlyRate*) in a virtual patient, comprising:

determining a fractional change in the insulin level of the virtual patient ($Fract\Delta_{insulin}$);

and

calculating the probability of a moderate or severe hypoglycemic event by solving the equation $HypoGlyRate(Fract\Delta_{insulin}) = a / (1 + \exp^{-(Fract\Delta_{insulin}-b)tc})$.

22. An apparatus for estimating a virtual patient's fasting plasma glucose (FPG) level, the apparatus comprising:

a virtual patient basal hepatic production determiner;

a virtual patient insulin level determiner; and

a virtual patient FPG level calculator coupled to said virtual patient basal hepatic production determiner and to said virtual patient insulin level determiner.

23. An apparatus for estimating if a virtual patient has developed symptoms of type 1 diabetes, the apparatus comprising:

a virtual patient genetic propensity to develop type 1 diabetes presenter; and

a virtual patient type 1 diabetes determiner coupled to said virtual patient genetic propensity to develop type 1 diabetes presenter.

24. An apparatus for estimating if a virtual patient has developed symptoms of type 2 diabetes, the apparatus comprising:

a virtual patient relative risk associated with body mass index determiner;

a virtual patient impaired glucose tolerance level determiner; and

a virtual patient type 2 diabetes determiner coupled to said virtual patient relative risk associated with body mass index determiner and to said virtual patient impaired glucose tolerance level determiner.

25. An apparatus for estimating a virtual patient's hemoglobin A_{1c} , the apparatus comprising:

a virtual patient fasting plasma glucose determiner; and

a virtual patient hemoglobin A_{1c} calculator coupled to said virtual patient fasting plasma glucose determiner.

26. An apparatus for estimating a virtual patient's randomly measured blood glucose, the apparatus comprising:

a virtual patient fasting plasma glucose determiner; and

a virtual patient randomly measured blood glucose calculator coupled to said virtual patient fasting plasma glucose determiner.

27. An apparatus for estimating a virtual patient's tolerance to an oral glucose load at age t , the apparatus comprising:

a virtual patient fasting plasma glucose determiner;

a virtual patient body mass index determiner;

a virtual patient systolic blood pressure determiner;

a virtual patient triglyceride level determiner; and

a virtual patient tolerance to an oral glucose load at age t calculator coupled to said virtual patient fasting plasma glucose determiner, said virtual patient body mass index determiner; said virtual patient systolic blood pressure determiner, and said virtual patient triglyceride level determiner.

28. An apparatus for estimating a virtual patient's thirst level at time x , the apparatus comprising:

a virtual patient fasting plasma glucose determiner;
a standard deviation of the degree of thirst experienced by an individual determiner; and
a virtual patient thirst level at time x and age t calculator coupled to said virtual patient fasting plasma glucose determiner and to said standard deviation of the degree of thirst experienced by an individual determiner.

29. An apparatus for estimating the probability of occurrence of diabetic ketoacidosis events for a virtual patient, the apparatus comprising:

a virtual patient untreated insulin level determiner; and
a virtual patient probability of occurrence of diabetic ketoacidosis events calculator coupled to said virtual patient untreated insulin level determiner.

30. An apparatus for estimating the probability of a moderate or severe hypoglycemic event in a virtual patient, the apparatus comprising:

a virtual patient insulin level fractional change determiner; and

a probability of a moderate or severe hypoglycemic event calculator coupled to said virtual patient insulin level fractional change determiner.

31. An apparatus for estimating a virtual patient's fasting plasma glucose (FPG) level, the apparatus comprising:

means for determining the virtual patient's basal hepatic production (FPG_0);

means for determining the virtual patient's insulin level (I); and

means for calculating the virtual patient's FPG at time t by solving the differential equation $FPG(t) = FPG_0 / (I * E)$, wherein E is a value representing efficiency of insulin use.

32. The apparatus of claim 31, wherein E is scaled such that $E = 1$ in the absence of diabetes and $0 \leq E \leq 1$ in the presence of diabetes.

33. The apparatus of claim 31, wherein for type 2 diabetes, a differential equation representing E is:

$$E(DF_2) = \left(a + b / (1 + (DF_2 / c)^d) \right)^{\frac{1}{2}}, \text{ wherein } DF_2 \text{ is a type 2 diabetes feature.}$$

34. The apparatus of claim 33,

$$\text{wherein } DF_2(t) = \left(1 - \exp \left(-a * IGT(\xi_3) / \left(1 + \exp \left(-\frac{(t-b)}{c} \right) \right) \right) \right) * RBMI(BMI) / \xi_2, \text{ wherein } a,$$

b , and c are constants, IGT is an impaired glucose tolerance value, and $RBMI$ is the relative risk associated with a person's body mass index (BMI).

35. The apparatus of claim 33, wherein the \overline{RBMI} is represented by:

$$RBMI_{\text{Women}}(BMI) = a + b / (1 + e^{-(BMI-c)/d}).$$

36. The apparatus of claim 33, wherein IGT is represented by:

$$IGT(\xi_3) = 2(1 - \xi_3),$$

wherein ξ_3 is a random value designed to cause the occurrence of diabetes in virtual patients to have the same types of interpersonal variations that occur in real people.

37. The apparatus of claim 31, wherein said means for determining said virtual patient's basal hepatic production in type 2 diabetes includes means for solving the differential equation

$FPG_0(t) = G(t) * H(DF_2(t))$, wherein $G(t)$ is the degree of insulin resistance in a person with diabetes (H).

38. The apparatus of claim 37, wherein $H(DF_2(t)) = 1 / (\text{MAX}[E^2(DF_2(t+a)), b])$.

39. The apparatus of claim 37, wherein

$G(t) = (a + bt^{1.5} - c * t^3 + \Delta_g) / (d - e \exp(-DF_2(t)\xi_2))$, wherein Δ_g represents a variance of basal hepatic production across individuals.

40. The apparatus of claim 31, wherein

$$I(DF_1, DF_2) = H(DF_2) * E(DF_2) / (1 + \exp((DF_1 - a)/b)).$$

41. An apparatus for estimating if a virtual patient has developed symptoms of type 1 diabetes, the apparatus comprising:

means for representing the virtual patient's genetic propensity to develop type 1 diabetes by a family history value *famhis*;

means for determining if the virtual patient has developed symptoms of type 1 diabetes at time *t* by solving the differential equation

$DF_1(t) = (1 - \exp(-\exp(a + bt + ct^2 + dt^3 + et^4 + ft^5)) * \text{famhis}) / \xi_1$, wherein *a*, *b*, *c*, *d*, *e*, and *f* are constants and ξ_1 is a random value.

42. An apparatus for estimating if a virtual patient has developed symptoms of type 2 diabetes, the apparatus comprising:

means for determining the virtual patient's relative risk associated with body mass index (RBMI);

means for determining the virtual patient's impaired glucose tolerance level (IGT); and

means for determining if the virtual patient has developed symptoms of type 2 diabetes at time *t* by solving the differential equation

$DF_2(t) = \left(1 - \exp \left(-a * IGT(\xi_3) / \left(1 + \exp \left(-\frac{(t-b)}{c} \right) \right) \right) \right) * RBMI(BMI) / \xi_2$, wherein *a*,

b, and *c* are constants.

43. The apparatus of claim 42, wherein the RBMI is represented by:

$RBMI(BMI) = a + b / (1 + e^{-(BMI-c)/d})$, wherein *BMI* is the virtual patient's body mass index.

44. The apparatus of claim 42, wherein IGT is represented by:

$$IGT(\xi_3) = 2(1 - \xi_3),$$

wherein ξ_3 is a random value.

45. An apparatus for estimating a virtual patient's hemoglobin A_{1c} (HbA_{1c}), comprising:

means for determining said virtual patient's fasting plasma glucose (FPG); and

means for calculating said virtual patient's hemoglobin A_{1c} by solving the

equation $HbA_{1c}(FPG) = a * FPG - b$, wherein a and b are constants.

46. An apparatus for estimating a virtual patient's randomly measured blood glucose (RPG), the apparatus comprising:

means for determining said virtual patient's fasting plasma glucose (FPG); and

means for calculating said virtual patient's randomly measured blood glucose by solving

the equation $RPG(FPG) = (a + b / (1 + \exp(-(FPG - c)d))) * \exp \Delta_{RPG}$, wherein a , b , c , and d are constants, and Δ_{RPG} is an uncertainty value.

47. An apparatus for estimating a virtual patient's tolerance to an oral glucose load at age t , comprising:

means for determining the virtual patient's fasting plasma glucose (FPG);

means for determining the virtual patient's body mass index (BMI);

means for determining the virtual patient's systolic blood pressure (SBP);

means for determining the virtual patient's triglyceride level (TRI); and

means for calculating the virtual patient's tolerance to an oral glucose load at age t by solving the equation:

$$OGT(t) = a * FPG(t) + bt + cBMI(t) + dSBP(t) + eTRI(t) - f + VAR_{OGT}$$

48. The apparatus of claim 47, wherein said means for determining the virtual patient's SBP may include means for multiplying a peripheral resistance for the virtual patient by a diabetes blood pressure factor ($DiabBP$), which is a function of a diabetes feature and higher for people with more severe diabetes.

49. An apparatus for estimating a virtual patient's thirst level at time x , the apparatus comprising:

means for determining the virtual patient's fasting plasma glucose (FPG);

means for determining a standard deviation (SD_{thirst}) of the degree of thirst experienced by an individual; and

means for calculating the virtual patient's thirst level at time x and age t by solving the equation $Thirst(x, FPG(t)) = \frac{1}{\sqrt{2\pi SD_{thirst}}} \exp\left(-\left(\frac{x - MeanSym_{thirst}(FPG(t))}{2SD_{thirst}}\right)^2\right)$.

50. An apparatus for estimating the probability of occurrence of diabetic ketoacidosis events (DKA_{time}) for a virtual patient, comprising:

means for determining the virtual patient's insulin level if left untreated; and

means for calculating the virtual patient's probability of occurrence of diabetic ketoacidosis events by solving the equation $DKA_{time} = \text{Max}(a / (1 + \exp(I_{untreated} - b) / c) d)$, wherein a , b , c , and d are constants.

51. An apparatus for estimating the probability of a moderate or severe hypoglycemic event (*HypoGlyRate*) in a virtual patient, comprising:

means for determining a fractional change in the insulin level of the virtual patient ($\text{Fract}\Delta_{insulin}$); and

means for calculating the probability of a moderate or severe hypoglycemic event by solving the equation $\text{HypoGlyRate}(\text{Fract}\Delta_{insulin}) = a / (1 + \exp^{-(\text{Fract}\Delta_{insulin} - b)tc})$.

52. A program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method for estimating a virtual patient's fasting plasma glucose (FPG) level, the method comprising:

determining the virtual patient's basal hepatic production (FPG_0);

determining the virtual patient's insulin level (I); and

calculating the virtual patient's FPG at time t by solving the differential equation

$FPG(t) = FPG_0 / (I * E)$, wherein E is a value representing efficiency of insulin use.

53. A program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method for estimating if a virtual patient has developed symptoms of type 1 diabetes, the method comprising:

representing the virtual patient's genetic propensity to develop type 1 diabetes by a family history value *famhis*;

determining if the virtual patient has developed symptoms of type 1 diabetes at time *t* by solving the differential equation

$DF_1(t) = (1 - \exp(-\exp(a + bt + ct^2 + dt^3 + et^4 + ft^5)) * famhis) / \xi_1$, wherein *a*, *b*, *c*, *d*, *e*, and *f* are constants and ξ_1 is a random value.

54. A program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method for estimating if a virtual patient has developed symptoms of type 2 diabetes, the method comprising:

determining the virtual patient's relative risk associated with body mass index (RBMI);

determining the virtual patient's impaired glucose tolerance level (IGT); and

determining if the virtual patient has developed symptoms of type 2 diabetes at time *t* by solving the differential equation

$$DF_2(t) = \left(1 - \exp \left(-a * IGT(\xi_3) / \left(1 + \exp \left(-\frac{(t-b)}{c} \right) \right) \right) \right) * RBMI(BMI) / \xi_2, \text{ wherein } a,$$

b, and *c* are constants.

55. A program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method for estimating a virtual patient's hemoglobin A_{1c} (*HbA_{1c}*), the method comprising:

determining said virtual patient's fasting plasma glucose (*FPG*); and

calculating said virtual patient's hemoglobin A_{1c} by solving the equation $HbA_{1c}(FPG) = a * FPG - b$, wherein a and b are constants.

56. A program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method for estimating a virtual patient's randomly measured blood glucose (RPG), the method comprising:

determining said virtual patient's fasting plasma glucose (FPG); and

calculating said virtual patient's randomly measured blood glucose by solving the equation $RPG(FPG) = (a + b / (1 + \exp(-(FPG - c)d))) * \exp \Delta_{RPG}$, wherein a , b , c , and d are constants, and Δ_{RPG} is an uncertainty value.

57. A program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method for estimating a virtual patient's tolerance to an oral glucose load at age t , the method comprising:

determining the virtual patient's fasting plasma glucose (FPG);

determining the virtual patient's body mass index (BMI);

determining the virtual patient's systolic blood pressure (SBP);

determining the virtual patient's triglyceride level (TRI); and

calculating the virtual patient's tolerance to an oral glucose load at age t by solving the equation:

$$OGT(t) = a * FPG(t) + bt + cBMI(t) + dSBP(t) + eTRI(t) - f + VAR_{OGT}$$

58. A program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method for estimating a virtual patient's thirst level at time x , the method comprising:

determining the virtual patient's fasting plasma glucose (FPG);

determining a standard deviation (SD_{thirst}) of the degree of thirst experienced by an individual; and

calculating the virtual patient's thirst level at time x and age t by solving the equation

$$Thirst(x, FPG(t)) = \frac{1}{\sqrt{2\pi SD_{thirst}}} \exp\left(-\left(\frac{x - MeanSym_{thirst}(FPG(t))}{2SD_{thirst}}\right)^2\right).$$

59. A program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method for estimating the probability of occurrence of diabetic ketoacidosis events (DKA_{time}) for a virtual patient, the method comprising:

determining the virtual patient's insulin level if left untreated; and

calculating the virtual patient's probability of occurrence of diabetic ketoacidosis events by solving the equation $DKA_{time} = \text{Max}(a/(1 + \exp(I_{untreated} - b)/c)d)$, wherein a , b , c , and d are constants.

60. A program storage device readable by a machine, tangibly embodying a program of instructions executable by the machine to perform a method for estimating the probability of a moderate or severe hypoglycemic event ($HypoGlyRate$) in a virtual patient, the method comprising:

determining a fractional change in the insulin level of the virtual patient ($Fract\Delta_{insulin}$);
and

calculating the probability of a moderate or severe hypoglycemic event by solving the
equation $HypoGlyRate(Fract\Delta_{insulin}) = a / (1 + \exp^{-(Fract\Delta_{insulin}-b)tc})$.